Region-specific burden of late preterm birth during the first week of life

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Abstract

Introduction: International data indicate that the number of late-premature babies (34-36.6 weeks) are on the increase.[1,2,3,4] Late preterm newborns also account for the largest subset of all preterm births (74%). With regard to South Africa, no information exists on the potential disease burden associated with a late preterm birth. Determining the disease burden related to late premature births is especially important since gestation is often inaccurate and weight criteria rather than gestation is used for discharge.

Aim: The primary objective was to document morbidity and mortality within the first week of life of late premature births at a tertiary hospital in the Western Cape, South Africa.

Methods: A prospective descriptive study of late-premature babies born at Tygerberg Hospital between 1 March and 31 May 2018 was performed. Babies admitted to both the neonatal and postnatal wards were included. Data was collected on day 1, 3 and 7 of life, with telephonic interview of the mother in the case of discharge. Obstetric data as well as demographic data, morbidity and mortality data was collected on the neonate. Specific interventions including need for admission, length of stay, respiratory support, surfactant administration, antibiotic prescription, poor feeding and jaundice were recorded.[3] Neonatal data was stratified according to gestation 34.0-34.6 vs 35.0-36.6 weeks, as the former is routinely admitted if neonatal capacity allows.

Results: 117 babies were enrolled, 63 in the 34-34.6 week group and 54 in the 35.0-36.6 weeks group. The primary obstetric reason for delivery was pre-eclampsia/eclampsia followed by spontaneous preterm labour. The median maternal age was 27.5 years in the younger gestational group and 29 years in the older group. There was a large variation in weight in both groups of babies, with the median weight in the 34-34.6 group being 1895g (Range 1428g-3695g), and in the older gestation being 2140g (Range 1030g- 5000g).

A total of 98 babies required admission to the neonatal service. In the younger gestation group, 62 babies (98.4%) were admitted, while 36 (66.7%) of the 35-36.6 week group required admission to the neonatal ward. The majority of the babies in both groups had respiratory distress, requiring nasal continuous positive airway pressure (nCPAP). None of the babies required surfactant treatment or invasive ventilation. Antibiotics were initiated in 46 of the admitted babies, 29 of them continuing by day 3. Ten (10.8%) babies developed jaundice on day 1 and 11 (11.9%) had documented hypoglycaemia. By day 3, 50% of the babies were not able to satisfactorily breastfeed. On day three of life, only 5 of the 117 infants were discharged home. Fifteen of the infants were still admitted only for maternal reasons, while 96 babies still required medical attention. By day 7, 54 babies (63.2% of original cohort) were still admitted for medical care and another 8 were only in hospital due to maternal reasons. None of the babies during the study period demised, however possible late neonatal death was outside the scope of this study.

Conclusion: There was a high burden of morbidity amongst the late-preterm group. In this specific group of babies, discharge policies should be reviewed.

Introduction

International data indicate that the number of late-premature babies (34-36.6 weeks) are on the increase.[1,2,3,4] There is however, variation across countries, with Nordic countries and the United States showing a decrease in late preterm birth rates between 2006 and 2014.[5] The disease burden associated with late premature birth appears to be of noteworthy clinical and public health importance due to the associated risks of adverse short (neonatal)- and long-term childhood outcomes. There is however, a data gap with regard to the disease burden imposed by the late preterm infant, especially from lower- and middle-income settings, which have to be explored and studied, in order to inform public health services.[6] With regard to South Africa, no data on the outcome of late-preterm babies exists. Determining the disease burden related to late premature births is especially important since gestation is often inaccurate and weight criteria rather than gestation is used for discharge. The primary objective was to document morbidity and mortality, within the first week of life, of late preterm infants born at Tygerberg Hospital.

Methods

Tygerberg Hospital is a referral level 2 and 3 Academic hospital situated in the East Metropole of Cape Town. The hospital drains roughly half the population of the Western Cape Province servicing both rural and urban areas. In 2016 there were 7793 babies born at Tygerberg Hospital of which 1951 were between 1500-2500g. Mothers and babies can be discharged as early as 6 to 24 hours after delivery if medically fit. Neonates with a birth weight < 1800g are routinely admitted to the neonatal wards. Neonates with a gestation of 35 weeks or less are considered for admission but may not be admitted if there are neonatal bed-space constraints and the baby is assessed as being well.

This was a prospective descriptive study.

Late preterm infants born at Tygerberg Hospital were recruited from both the postnatal wards as well as the neonatal wards from March till May 2018.

Gestational age was calculated based on early antenatal ultrasound (EUS) performed before 24 weeks gestation. Where EUS was not available, gestation was determined by foot length, using the foot length chart, previously validated at Tygerberg Hospital.[7] Babies were excluded from the study where consent could not be obtained or where the baby was known to have a genetic abnormality. Information was collected on day 1, day 3 and day 7 from the maternal and neonatal records using a structured questionnaire. In the case of discharge, the mothers were interviewed telephonically on day 3 and/or day 7 using the structured questionnaire.

Maternal data obtained included age, gravida and parity, complications related to the pregnancy, comorbid diseases including syphilis and HIV infection, and whether the mother received antenatal steroids. Further information concerning the reasons for delivery, the method of delivery and complications during the delivery were collected. Indication for hospitalization of the mother and duration of hospitalization were recorded.

Neonatal data that was collected included the gestational age, birth weight, APGAR score of the baby and any morbidity and mortality that arose during the first seven days of life. In keeping with international findings,[8] specifically the following complications (morbidity) were sought: hypothermia (temperature below 36.5°C), hypoglycaemia (where blood glucose is less than 2.6mmol/litre using point-of-care device), respiratory distress, presumed or possible infection prompting the initiation of antibiotics by attending doctor, poor feeding (as assessed

and documented by the attending doctor) and neonatal jaundice requiring phototherapy or exchange transfusion as per the Tygerberg Hospital jaundice guidelines.[9]

Data management

Ethical approval was obtained from both Stellenbosch University and the Western Cape Department of Health. The Biostatical department of Stellenbosch University assisted us in calculating the sample size required. On enrolment each baby/mother pair received a study number which was uncoupled from the folder number and any other identifying information. Data was collected on a standardized Google doc document and imported into Excel. The data was stored on a password-protected Excel spreadsheet and analyzed by the researcher using Excel.

Statistical considerations

Sample size calculation

In deciding the necessary sample size, we used the South African Perinatal Problem Identified Programme (PPIP) data[10] to estimate the number of late preterm babies born at Tygerberg Hospital annually. PPIP uses weight categories and not gestational age. We used the weight categories 1.5-2.5kg as this correlate best to late preterm infants, 34- 36 weeks 6 days gestation.

There were no studies found that stated the readmission rate for late preterm infants in South Africa therefore we used a study from Cincinnati, Ohio, that had a 3.6% readmission rate[11] and estimated that we would have at least a 10% readmission rate being a developing county.

Assuming a 10% readmission rate and using a 5% confidence interval we estimated that we needed a minimum of 130 patients. It is estimated that this is the number of late preterm babies born in a 3 month period.

Results

A total of 121 infants were collected. Four were disqualified, due to differences in gestation recorded in labour ward and nursery. Of the remaining 117 infants, 69 were born via

caesarean section, 45 were born via normal vaginal delivery and 3 with Vacuum delivery. There were 3 sets of twins.

Of the 117 babies enrolled, 63 were in the 34-34.6 age group and 54 in the 35-36.6.

Maternal Data

The median maternal age was 27.5 years (Interquartile range 22.5-34.5) in the 34.0-34.6 gestational age group and 29 years (Interquartile range 18-44) in the 35.0-36.6 gestational age group.

Of the 114 mothers 22 were HIV-infected, 19 were on antiretroviral drugs at time of delivery.

Only 3 mothers had syphilis, none of them were fully treated.

Antenatal steroids were given in 29/61 mothers in the 34-34.6 gestation, 18 of these babies required CPAP at birth. However, the number and interval of steroid doses were not explored in this study.

The majority of the babies were delivered due to pre-eclampsia or spontaneous preterm labour (Table 1). In some pregnancies there was more than one indication for delivery.

Table 1: Maternal Reasons for delivery

Maternal reasons for delivery	34.0-34.6 weeks gestation (n=61)	35.0-36.6 weeks gestation (n=53)
Hypertension	5	5
Chorioamnionitis	2	1
Pre-eclamptic toxemia	31	14
Spontaneous labour	21	23
Diabetes Mellitus	4	2
Infection (other)	4	4
Caesarean section for twins	4	2
Other	6	9

Neonatal data

There was a large variation in weight in both groups of babies (Figure 1 and 2), with the median weight in the 34-34.6 group being 1895g (Range 1428g-3695g) (IQR 1735g – 2130g), and in the older gestation being 2140g (Range 1030g- 5000g) (IQR 1875g – 2615g).

Figure 1: Weight distribution at birth 34.0 -34.6 weeks gestation

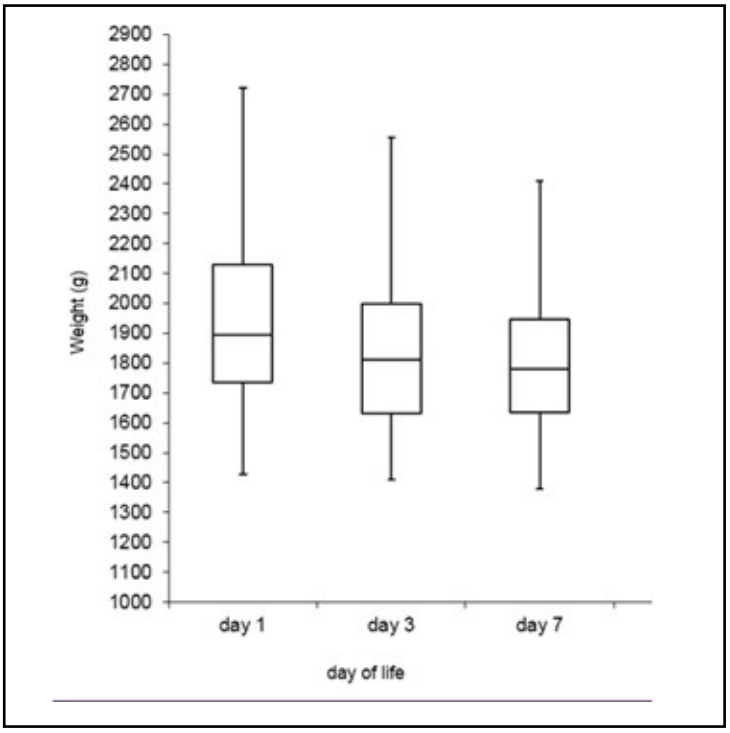
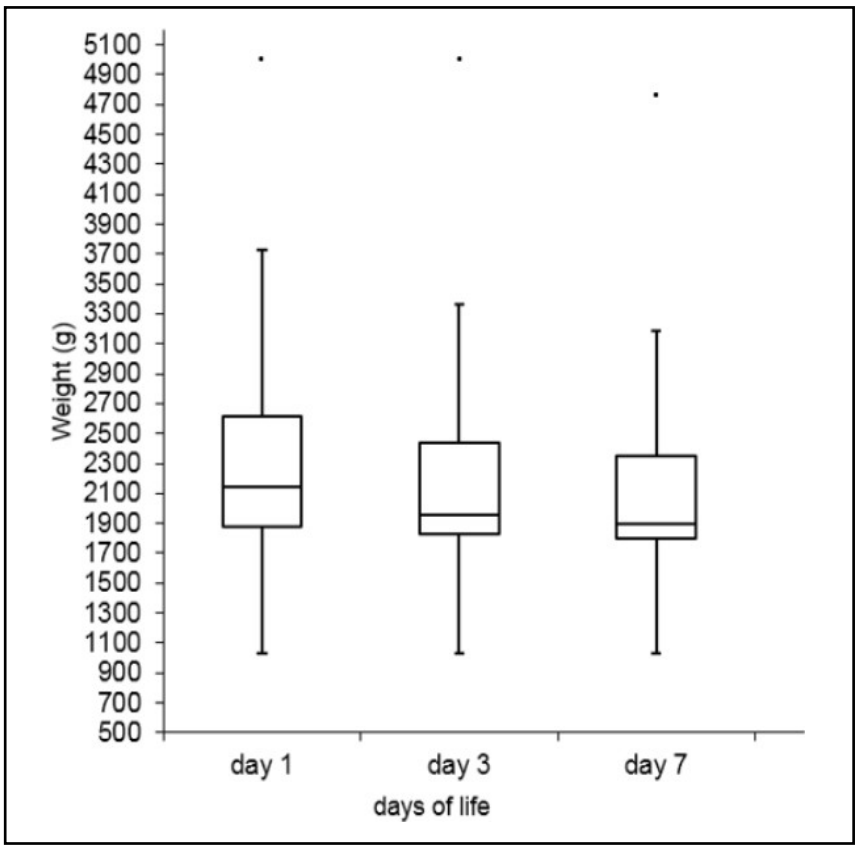


Figure 2: Weight distribution at birth 35.0 -36.6 weeks gestation



Of the 117 babies, 98 required admission to the neonatal service for medical care. Of the 34-34.6 weeks gestation group 62 babies (98.4%) were admitted, while 36 (66.7%) of the 35-36.6 week group required admission to the neonatal ward. Only 21 babies in the younger gestation and 8 babies in the older gestation group had a birthweight <1800g.

Many babies had more than one diagnosis on admission. More than half the babies in both groups had respiratory distress, with the majority of these babies requiring nCPAP or nasal prong oxygen (Table 2 and 3).

Table 2: Diagnosis on admission

Diagnosis on admission	34.0-34.6weeks gestation (n=63)	35.0-36.6 weeks gestation (n=54)
Total number of babies requiring admission (%)	62 (98.4%)	36 (66.7%)
Jaundice	7	3
Hypoglycaemia	5	6
Respiratory Distress	30	20
Hypothermia	0	1
Possible sepsis	31	15
Inadequate feeding	7	4
Other	1	3

Table 3: Interventions on admission

Intervention required	34.0-34.6 (n=63)	35.0-36.6 (n=54)
nCPAP	27	14
NPO2	3	7
Intubation	0	0
Ventilation	0	0
IV antibiotics	31	15
Surfactant	0	0

On day three of life, only 5 of the 117 infants were discharged home. Fifteen of the infants were still admitted only for maternal reasons, while 96 babies still required medical attention. By day 7, 54 babies (63.2% of original cohort) were still admitted for medical care and another 8 were only in hospital due to maternal reasons. None of the babies required readmission once discharged during the first 7 days of life.

Table 4: Medical reason and interventions for still being admitted on day 3 and day 7

	34-34.6 weeks (n=63)		**35-35.6 weeks (n=54)**	
	Day 3	**Day 7**	**Day 3**	**Day 7**
Number discharged	1	7	5	21
Number admitted only for maternal reasons	0	1	15	8
Number admitted for medical reasons	62	54	34	20
Medical reasons for admission				
Jaundice	19	22	11	5
Hypoglycaemia	1	1	3	1
Respiratory distress	23	6	12	2
Hypothermia	0	0	1	0
Inadequate feeding	37	26	22	4
Presumed infection	20	3	11	3
Other	1	3	3	2
Interventions				
Nasal prongs	11	4	9	2
NCPAP	12	2	3	0
IV antibiotics	17	3	11	3
Surfactant	2	0	0	0
Invasive ventilation	0	0	0	0

Discussion

There was a high admission rate to the neonatal ward. This may in part be due the protocol at Tygerberg Hospital where all less than 35 week old babies and/or less than 1800g, babies are admitted to the neonatal service. However, the majority of the babies in both gestation groups required intervention, implying that weight and gestation are not the only reason for admission. Even in the later gestation group, where only 7 of the 55 babies had a weight below the mandatory admission weight of 1800g, 36 of the babies required admission.

The primary obstetric reason for premature delivery was pre-eclampsia in the early group and spontaneous labour in the later gestation group. This is not unexpected as Tygerberg Hospital is the tertiary referral centre and mothers with pre-eclampsia are routinely referred.

There was a very large variation in weight between the babies ranging from 1030g to 5000g. This could potentially be due to the fact that this study was done at a tertiary hospital and therefore the small for gestational age and large for gestational age baby would be more common due to maternal reasons.

When looking at the number of babies discharged on day three of life, only 6 babies had gone home. By day 7, 74 babies were still admitted for medical care, highlighting the high morbidity associated with this group.

The main reason for admission was respiratory distress requiring mainly nCPAP. While the cause of respiratory distress was not investigated in this study, it is assumed that the majority of these cases are due to Respiratory Distress Syndrome (RDS) especially in the lower gestation group.[12,13] Of the 92 admissions, 51 required some respiratory support on day 1 (mainly nCPAP), with 45 still requiring support on day 3 and 8 on day 7. Surprisingly, only 2 babies required surfactant administration by day 3 and none required invasive ventilation. It is well known that the early use of nCPAP decreases the need for surfactant.[13] This emphasizes the need for access to nCPAP at smaller district and rural hospitals where nCPAP is not currently readily available as these babies may be delivered and managed there. About a third of the babies developed jaundice during the first week of life. Of note is that 10% of babies were found to be jaundiced on the first day of life. This raises concern for babies born at smaller birthing units where they are routinely discharged after a few hours of life.

Prematurity together with poor feeding and undetected jaundice raises the risk for severe hyperbilirubinemia.

Feeding difficulties are not unexpected in this group of babies, the large number of babies where this was found, even in the older gestation group, is still concerning. By day 3, 58.7% in the younger gestation and 40.7% of the older group were still reported to have feeding difficulties. We acknowledge that the fact that this study was done at a tertiary hospital may influence the results as the maternal illness may delay the initiation of breastfeeding. However, once again the high number of babies struggling to adequately feed does raise concern for late premature babies delivered at birthing units or smaller hospitals where they may be sent home within a few hours. Ensuring that adequate breastfeeding is established, before discharge of mother and baby needs to be emphasised, together with close monitoring of weight and feeding in these babies after discharge.

There was a high rate of antibiotic use in the babies on admission. This is most likely in keeping with the prophylactic use of antibiotics in all babies delivered due to spontaneous preterm labour until sepsis is ruled out by 48hours of life. By day 3, 23.9% of babies were still being treated for possible or presumed sepsis. By day 7 only 6 of the babies were on antibiotics. It was beyond the scope of this study to determine whether this was ongoing from birth or whether antibiotics were initiated for new-onset sepsis. 11 babies (10%) had hypoglycaemia on admission, which highlights the need for glucose monitoring in this high-risk group, and requires heightened awareness across facilities where these babies may be delivered.

Strengths and weaknesses of this study

This was a prospective study and the first of its kind in South Africa. Babies admitted both to the postnatal wards with their mothers as well as those admitted to the nursery were included, making it a more representative sample. However, this pilot study was performed in a tertiary hospital which will impact the findings. Also, the study was designed as a descriptive study since there is currently no data on morbidity in these babies in South Africa. While the numbers were not large enough for detailed statistical analysis, we were able to demonstrate important trends in the outcomes of these babies. Further studies will need to

be performed across all levels of care where these mothers and babies may present, so that management and discharge protocols can be reviewed.

Contributions of the study

The large burden of preterm births calls for research to understand mechanisms and interactions of risk factors, and to develop more effective interventions for primary prevention. Immediate and major effects are possible by improving the clinical care of preterm newborn babies.

In our study there was a high burden of morbidity amongst the late-preterm group. While this study was performed in a tertiary setting with high-risk mothers and babies, it is important that similar studies are undertaken at the primary care birthing units where these babies would be discharged within 6 hours after delivery, largely based on weight criteria. In this specific group of babies, discharge policies should be reviewed

Contribution of the authors

Article submission by Dr Magriet van Niekerk as MMed project (Stellenbosch University), as a prerequisite with Health Professions Council of South Africa for registration as a Paediatrician.

MSvN: Conceptualisation of study, submission to ethics committees, data collection, data management and analysis. Writing of the article.

HH: primary supervisor, assisted with data analysis, editing and approval of final version.

JS: secondary supervisor: editing and approval of final version

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